REMARKS

This amendment adds, changes and/or deletes claims in this application. For all claims that are or were in the application, regardless of whether the claim(s) remain under examination in the application, a detailed listing of is presented, with appropriately defined status identifiers. Thus, claims 1-60, 66, 69-76, 78-81 and 83-89 have been cancelled. Claims 61-64, 67, 68, 77 and 82 are currently amended, and claim 91 is added.

Upon entry of this response, claims 61-65, 67, 68, 77, 82 and 90-91 will be pending. Additionally, paragraphs in the specification have been amended on pages 2 and 3.

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. OBJECTIONS TO SPECIFICATION

The examiner has objected to the use of Ciphergen trademarks in the specification. Applicants believe the revisions advanced here obviate the objection.

The examiner also asserts that the specification does not provide antecedent support for claim 90. Applicants point the examiner to page 3, bottom of ¶ 3.

II. REJECTIONS UNDER 35 U.S.C. § 112 ¶2

The examiner rejects claims 45, 46, 52, 61, 82 and 89 for alleged indefiniteness. Applicants believe the present amendment obviates the rejection.

The examiner also rejects claim 51 for alleged indefiniteness, asserting that it is unclear whether the term "hydrophobic adsorbent" "refers to an adsorbent that is purely hydrophobic or an adsorbent that has hydrophobic portions." Applicants respectfully disagree. The specification provides that a hydrophobic adsorbent denotes in one aspect an H4 probe, which comprises a C-16 aliphatic chain having an isopropyl functionality. *See, e.g.*, Application, ¶¶ 21 & 33. The specification further identifies as an exemplary hydrophobic adsorbent an H50 probe, which comprises a C9 aliphatic hydrocarbon chain attached to a phenyl ring. *See* paragraph spanning pg. 2-3. Moreover, as the examiner pointed out, it is well known in the art that hydrophobic adsorbents can derive their hydrophobicity from functional groups. *See* Pham (US 2002/0060290), ¶¶ 74-75. Accordingly, a

practitioner reviewing the specification would recognized readily that the term encompasses adsorbents having hydrophobic portions. Thus, the term is definite.

The examiner also rejects claims 77 and 82 under 35 U.S.C. § 112 ¶2 for alleged indefiniteness, asserting that the term "qualifying" is unclear allegedly because the specification does not define the term. Contrary to this assertion, however, the specification need not define every term appearing in the claims. Rather, §112 ¶2 requires only that one skilled in the art understand the metes and bounds of the claim when read in light of the specification. *See Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576 (Fed. Cir. 1986). The requisite precision is readily satisfied in this case.

The term "qualify" means "to describe by enumerating the characteristics or qualities of; characterize." *See, e.g.* THE AMERICAN HERITAGE DICTIONARY OF THE ENGLISH LANGUAGE, FOURTH EDITION, Houghton Mifflin Company, 2004. Thus, from the plain meaning of the terms, one of ordinary skill would recognize readily that claims 77 and 82 are directed to methods of characterizing the risk of preterm delivery and, thereby, understand the metes and bounds of the claims. Accordingly, the claim language satisfies §112 ¶2, and the rejection should be withdrawn.

III. REJECTIONS UNDER 35 U.S.C. §102

The examiner rejects claims 45-47, 59-60, 77 and 79 for alleged anticipation by Hitomi et al. (US 5,976,832). Applicants respectfully traverse the rejection.

Contrary to the examiner's assertion, Hitomi does not teach detecting intra-amniotic inflammation or qualifying the risk of preterm delivery by analyzing amniotic fluid for at least one calgranulin. At most, Hitomi merely suggests a possibility that assaying for CAAF1 might be useful for diagnosing generally a variety of indications such as cancer and inflammatory diseases. Thus understood, Hitomi provides an invitation to explore the clinical relevance of assaying for CAAF1. Moreover, Hitomi does not even hint at, for example, a method for diagnosing intra-amniotic inflammation in a patient, comprising analyzing a sample of amniotic fluid for the presence of at least biomarkers HNP-1, HNP-2, calgranulin A and calgranulin C. Accordingly, Hitomi does not contain each and every element of the claimed invention and, therefore, cannot anticipate the claims.

IV. REJECTIONS UNDER 35 U.S.C. § 103

The examiner rejects claims 45-59, 61-76, 78, 80-85 and 88-90 over combinations of a variety of documents, including Hitomi, Krone et al., Pham, Heine et al., Burke et al., Parker, and Woodruff. Applicants respectfully traverse the rejection.

The examiner has failed to demonstrate that the prior art references, when combined, teach or suggest all the claim limitations. Furthermore, the examiner has not shown that the references evince a motivation to combine or the requisite expectation of success. Therefore, the examiner has failed as a matter of law to establish a *prima facie* case of obviousness.

The failings of the primary reference, Hitomi, are described above. Regarding the secondary references, the examiner cites Krone for teaching the use of a BIAcore CM5 biosensor chip in conjunction with MALDI analysis. Pham is cited for teaching the use of Ciphergen's H4 PROTEIN CHIP.

The examiner cites Heine for allegedly teaching the use of an ELISA with monoclonal antibodies directed to HNP1-3 to screen for inflammatory diseases. The cited Heine, however, discloses only one monoclonal antibody, D1-1, and suggests that this antibody can be used to collectively capture defensins HNP1-3. Thus, Heine suggests detecting inflammatory diseases by measuring for the collective presence of HNP1-3. Heine does not teach, as asserted by the examiner, analyzing a sample of amniotic fluid for inflammation by analyzing the sample for the presence of each of HNP-1 and HNP-2.

The examiner cites Burke for teaching immunoassay instructions and Parker for teaching the determination of white blood cell count. Woodruff is cited for teaching that a white blood cell count of greater than 50 cells/mm^3 is indicative of a microbial invasion of the amniotic cavity.

Yet, the examiner has not shown that any combination of the cited references yields a method for diagnosing intra-amniotic inflammation in a patient, comprising analyzing a sample of amniotic fluid from a patient for the presence of each of at least biomarkers HNP-1, HNP-2, calgranulin A and calgranulin C and correlating the presence of one or more of the biomarkers with intra-amniotic inflammation. Likewise, no combination of the references produces a method for qualifying the risk of preterm delivery in a pregnant patient, comprising analyzing a sample of amniotic fluid from said patient for the presence of each of at least biomarkers HNP-1, HNP-2, calgranulin A and calgranulin C and correlating the presence of one or more of the biomarkers with a risk of preterm delivery.

Furthermore, the examiner has not established some suggestion or motivation to combine the references. For example, in combining the assays of Hitomi and Heine, the examiner asserts that "[t]he ability to detect an analyte that is stable and does not degrade provides the motivation to combine the detecting step of Heine et al[.] with the method of Hitomi et al." Office Action, pg. 10, ¶ 2. The proposed basis evinces only an apparent characteristic of Heine's analyte (HNP1-3) and not a motivation to combine Heine's detection of HNP1-3 with Hitomi's proposed detection of CAAF1. The examiner points to nothing, for example, in Hitomi that suggests that Hitomi's proposed analyte, CAAF1, is unstable or that Hitomi's assay should measure additional, more stable analytes.

Finally, the examiner has not established a reasonable expectation of success in combining the references to reach the claimed invention. For example, conventional wisdom forecloses a reasonable expectation of detecting the presence of each of at least biomarkers HNP-1, HNP-2, calgranulin A and calgranulin C because Heine's antibody is incapable of distinguishing HNP-1, HNP-2 or HNP-3.

Therefore, the examiner has failed as a matter of law to establish a *prima facie* case of obviousness.

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Applicants submit that the present application is in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. Examiner Lum is invited to contact the undersigned directly, should he feel that any issue warrants further consideration.

The Commissioner is authorized to charge any additional fees, which may be required regarding this application under 37 CFR §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the unpaid amount to the same deposit account. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 CFR §1.136 and authorize payment of any such extensions fees from the deposit account.

Respectfully submitted,

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